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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,099	01/20/2004	Timothy J. O'Leary	AFIP 03-16 01	4916

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OFFICE OF THE STAFF JUDGE ADVOCATE
U.S. ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
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EXAMINER	
CALAMITA, HEATHER	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 08/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/759,099	O'LEARY ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *04/27/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II, claims 4-14 in the reply filed on July 28, 2006, is acknowledged. The traversal is on the ground(s) that the rules of practice require the inventions restricted must be found to be both independent and distinct in order for a restriction requirement to be proper. Applicants argue search and examination of the entire application would not impose a serious burden on the office. This is not found persuasive because the search for the methods and products are not coextensive. The search of the method would require a text search of the method steps in addition to the components necessary to complete the steps which are not required for the search of the immunoliposome. Further, even if the immunoliposome were known, the method for using the immunoliposome may be novel and unobvious in view of the preamble or active steps. The search of the methods (groups II and III) is also not coextensive because as previously stated in the Office Action mailed July 12, 2006, they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation and therefore would require a separate search of the art. The immunoliposome-nucleic acid amplification assay (group II) involves amplification and detection steps and does not involve forming unilamellar vesicles. The method of forming an immunoliposome (group III) involves forming unilamellar vesicles and liposomes and does not involve amplification or detection. A search of the prior art for group II clearly would not encompass a search of the prior art for group III. An examination of all of the groups on the merits would require performing multiple searches of the prior which places a serious burden on the office, therefore the requirement is still deemed proper and is therefore made ***FINAL***.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al. (Anal. Chem., 2000, cited in the IDS) in view of Wu et al. (Letters in Applied Microbiology, 2001, cited in the IDS).

With regard to claim 4, Singh et al. teach a method for immunoliposome assay comprising

a) encapsulating a markers within the liposomal bilayers (see p. 6020 col. 1 lines 16-18 and p. 6021 Figure 2)

b) associating selected receptors to the liposomal bilayers (see p. 6020 col. 1 lines 8-14 and p. 6021 Figure 2)

c) exposing the selected receptors to target analytes which bind to the liposomal bilayer associated selected receptors (see p. 6021 Figure 2, where the target analyte is the toxin)

d) removing unbound liposomal bilayers (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 14-18)

e) lysing the bound liposomal bilayers to release the markers (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 18-20)

g) detecting the markers (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 20-23)

With regard to claim 5, Singh et al. teach the target analytes are antigen and further comprising the step of immobilizing the target antigens on a substrate (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-7)

With regard to claim 6, Singh et al. teach the substrate is a microtiter plate and the receptors are antibodies specific to the immobilized target antigen (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-7).

With regard to claim 7, Singh et al. teach further comprising indirectly binding the analyte to the substrate (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-7).

With regard to claim 8, Singh et al. teach the receptors are gangliosides incorporated into the liposomal bilayer and the analyte is an antigen (see p. 6020 col. 1 lines 8-14 and p. 6021 Figure 2).

With regard to claim 10, Singh et al. teach the step of quantifying the amount of analyte present (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 20-23, where the amount of fluorescence correlates with the amount of analyte).

With regard to claim 11, Singh et al. teach the analyte is a biological toxin (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-7).

With regard to claim 12, Singh et al. teach an immunoliposome assay method comprising

a) selecting a substrate having primary antibodies attached thereto (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-23)

b) exposing the substrate to a target analyte containing sample (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-23)

c) permitting the target analyte to bind to the primary antibodies attached to the substrate (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-23)

d) removing all unbound analyte (see)

e) exposing the bound analyte to immunoliposomes where the immunoliposomes couple with the analyte (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-23)

f) removing any uncoupled immunoliposomes (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-23)

g) rupturing the coupled immunoliposomes to release the markers (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-23)

i) detecting the markers representative of the target analyte (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-23)

With regard to claim 13, Singh et al. teach the steps of attaching the primary antibodies to the substrate and removing all unattached primary antibodies (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 1-7).

With regard to claim 14, Singh et al. teach the analyte is a biotoxin where the immunoliposomes are ruptured using detergent and the markers are quantified (see p. 6022 col. 1 under Fluoroimmunoassay for Tetanus, Botulinum and Cholera Toxins, lines 18-23, where the detergent is Triton X-100 and the fluorescence is quantified).

Singh et al. do not teach all of the limitations of claims 4-14, specifically with regard to claim 4, Singh do not teach step a) encapsulating a plurality of identical nucleic acid segments within the liposome step f) subsequently amplifying the nucleic acid segments and step g) detecting the released nucleic acids.

With regard to claim 9, Singh do not teach the nucleic acid segments are amplicons that are amplified using PCR.

With regard to claim 12, Singh do not teach step e) the immunoliposomes contain amplicons, step g) releasing the amplicons form the immunoliposomes and step h) amplifying the amplicon population using PCR.

With regard to claim 14, Singh do not teach the quantifying the amplicons by gel electrophoresis.

With regard to claim 4 step a), Wu et al. teach using nucleic acids as reporters for amplification, f) amplifying the nucleic acids and g) detecting the nucleic acids as an indication of the presence of the analyte (see p. 322 col. 2 under Immuno-PCR assay lines 9-28 and p. 323 Figure 1).

With regard to claim 9, Wu et al. teach the nucleic acids are amplified using PCR (see p. 322 col. 2 under Immuno-PCR assay lines 9-28).

With regard to claim 12, Wu et al. teach e) and g) using nuclei acids as reporters and h) amplifying the nucleic acid reporters using PCR (see p. 322 col. 2 under Immuno-PCR assay lines 9-28).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the immunoliposome assay as taught by Singh et al. with nucleic acid reporters, as taught by Wu et al. in order to detect the presence of an analyte in a sample with greater sensitivity than possible with standard immunoassay and fluorescence detection methods. Wu et al. state, "...the method described here demonstrates that immuno-PCR technology greatly extends the sensitivity of immunoassays. This hybrid technology exhibited analyte detection from 100 to 1000 fold better than the ELISA method performed with the same antibodies. Immuno-PCR technology, in principle, provides the basis for a new generation of sensitive immunoassays and may be useful in clinicopathological assays as well as detection of low level antigens (see p. 325 col. 1 first full paragraph)." An ordinary practitioner would have been motivated to substitute the markers in the immunoliposome assay as taught by Singh et al. with nucleic acid reporters, as taught by Wu et al. in order to improve the sensitivity of the immunoliposome assay. The DNA reporters disclosed by Wu enable detection of analytes present in a sample at very low levels because the DNA markers improve sensitivity from 100 fold to 1000 fold over standard immunoassay methods, therefore the ordinary practitioner would expect a markedly higher degree of sensitivity in the immunoassay if the traditional fluorescence markers were substituted with the DNA reporters.

Summary

3. No claims were allowable.

Correspondence

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

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hgc

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PRIMARY EXAMINER

Teresa Strzelecka
8/11/06